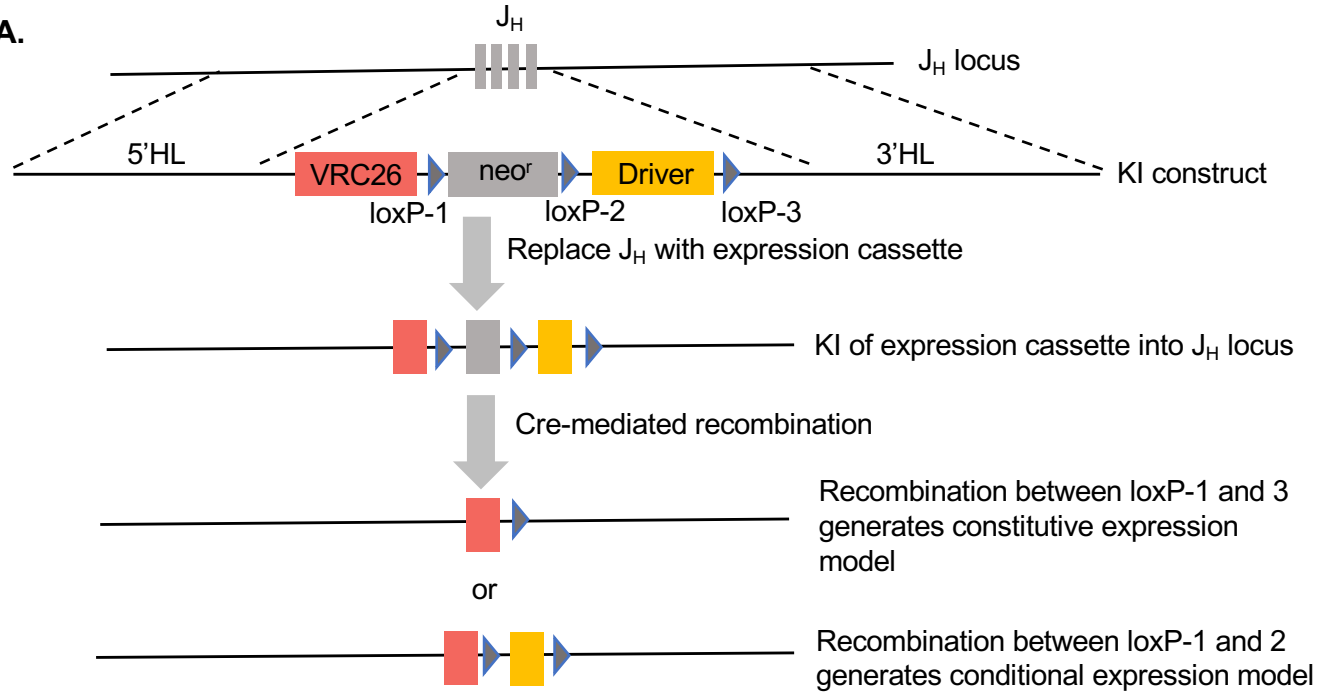


Figure S1

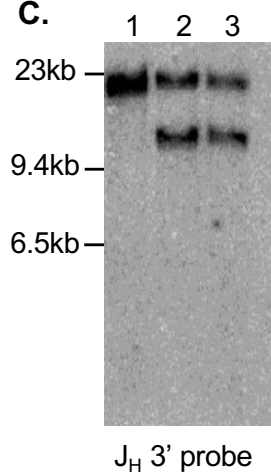
A.



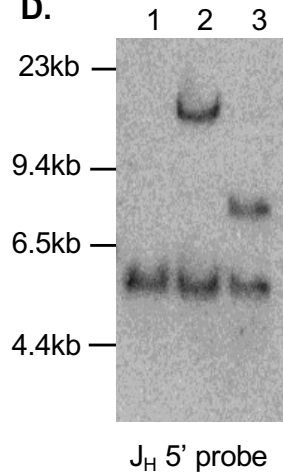
B.

Digest	Probe	Germline	Constitutive model	Conditional model
EcoRV	J_H 3'	16,530bp	10,808bp	10,968bp
NheI	J_H 5'	5,509bp	13,863bp	7,729bp
EcoRV+SpeI	J_k 3'	8,653bp	5,502bp	5,502bp
PstI	J_k 5'	7,006bp	5,263bp	5,263bp

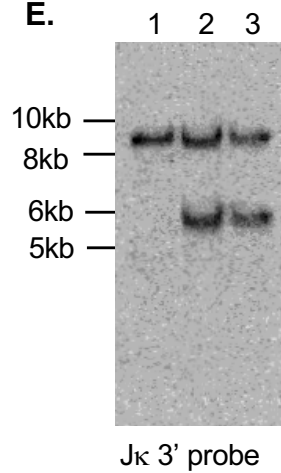
C.



D.



E.



F.

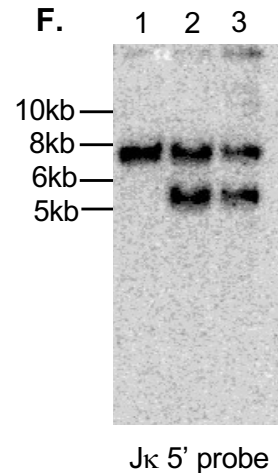


Figure S2

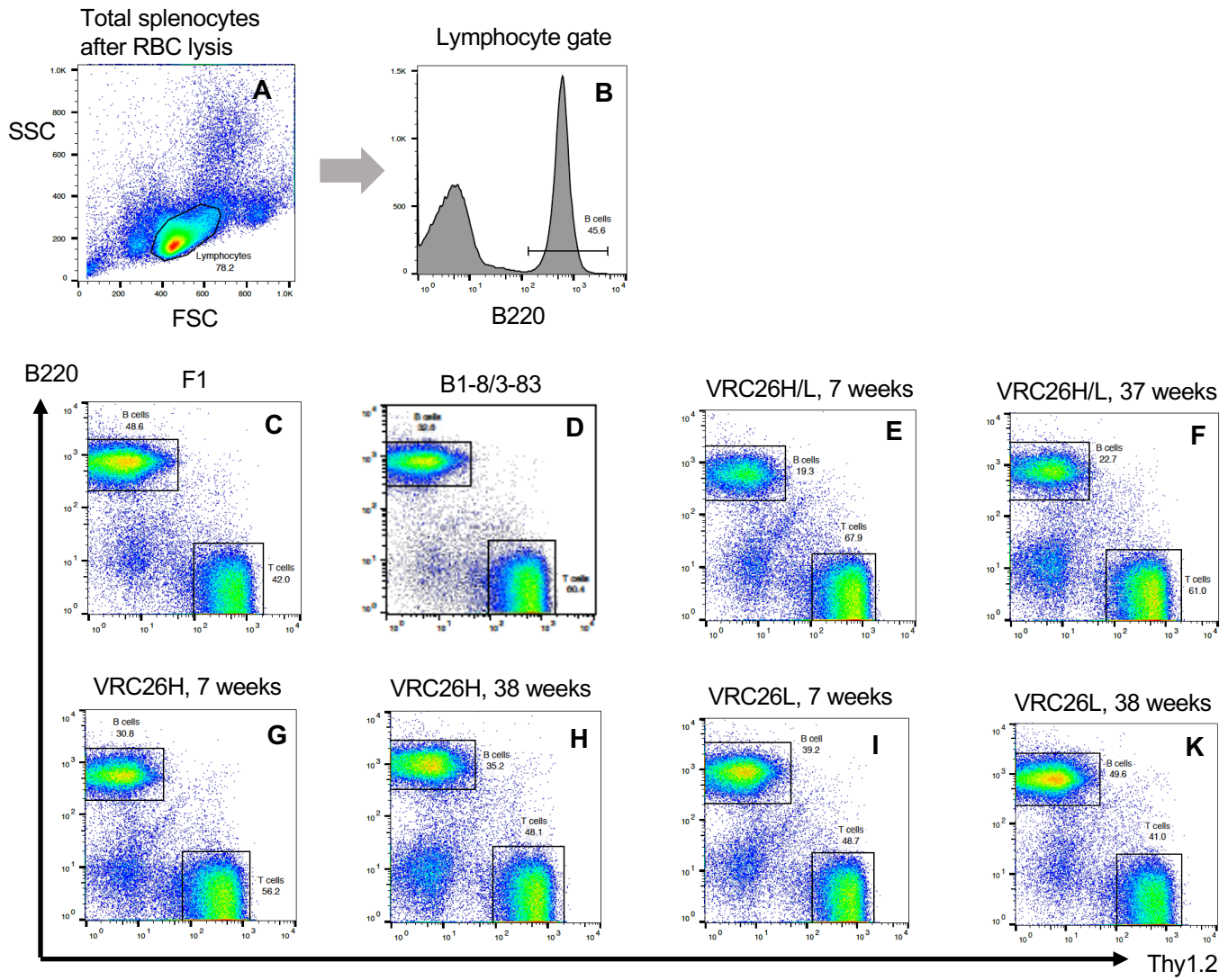


Figure S3

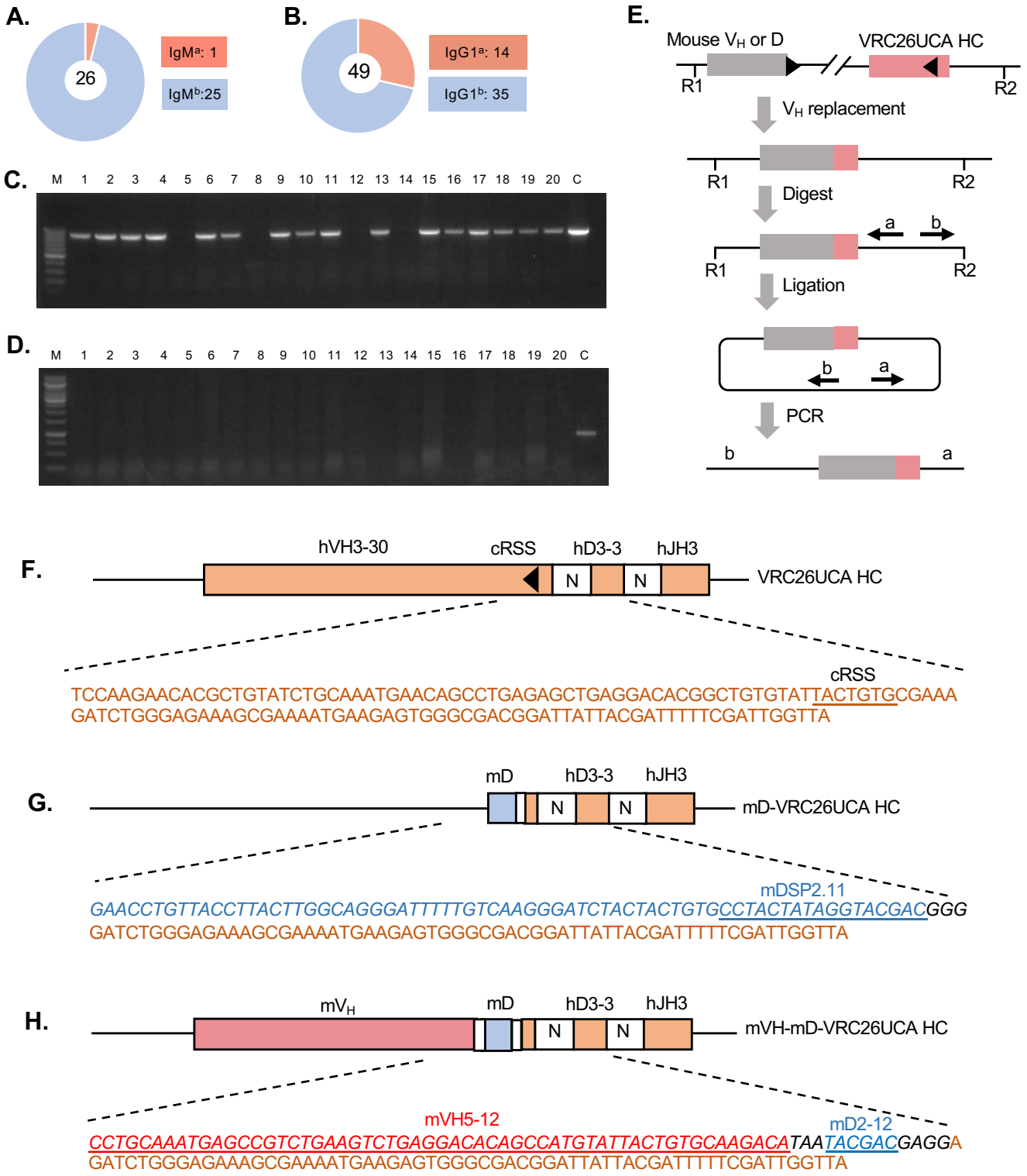


Figure S4

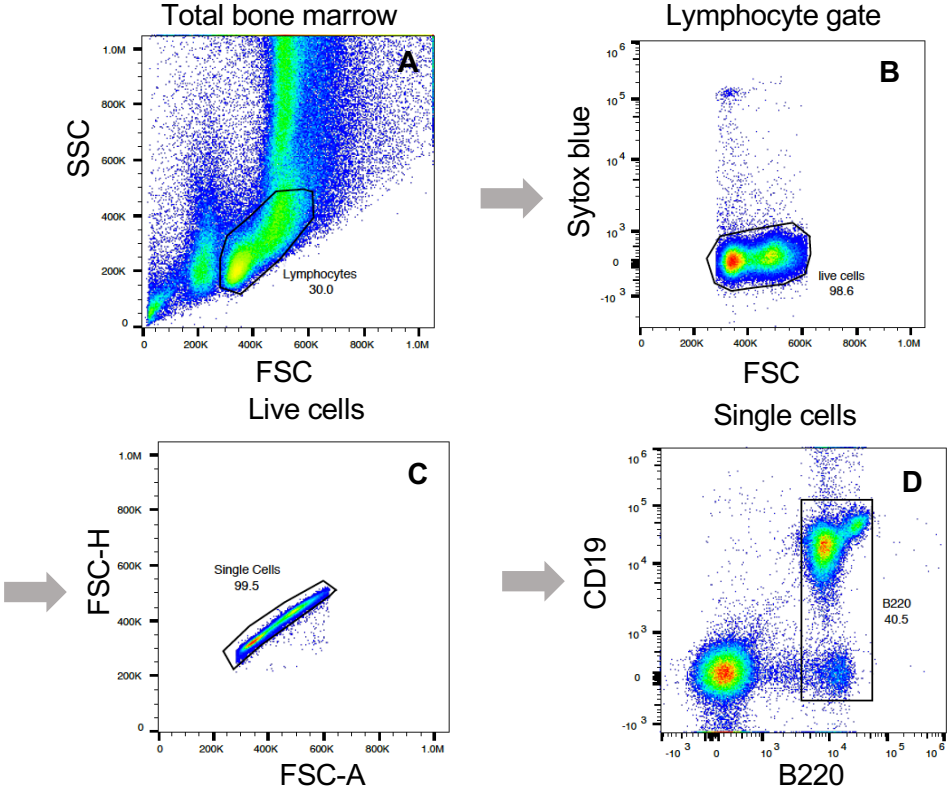


Figure S5

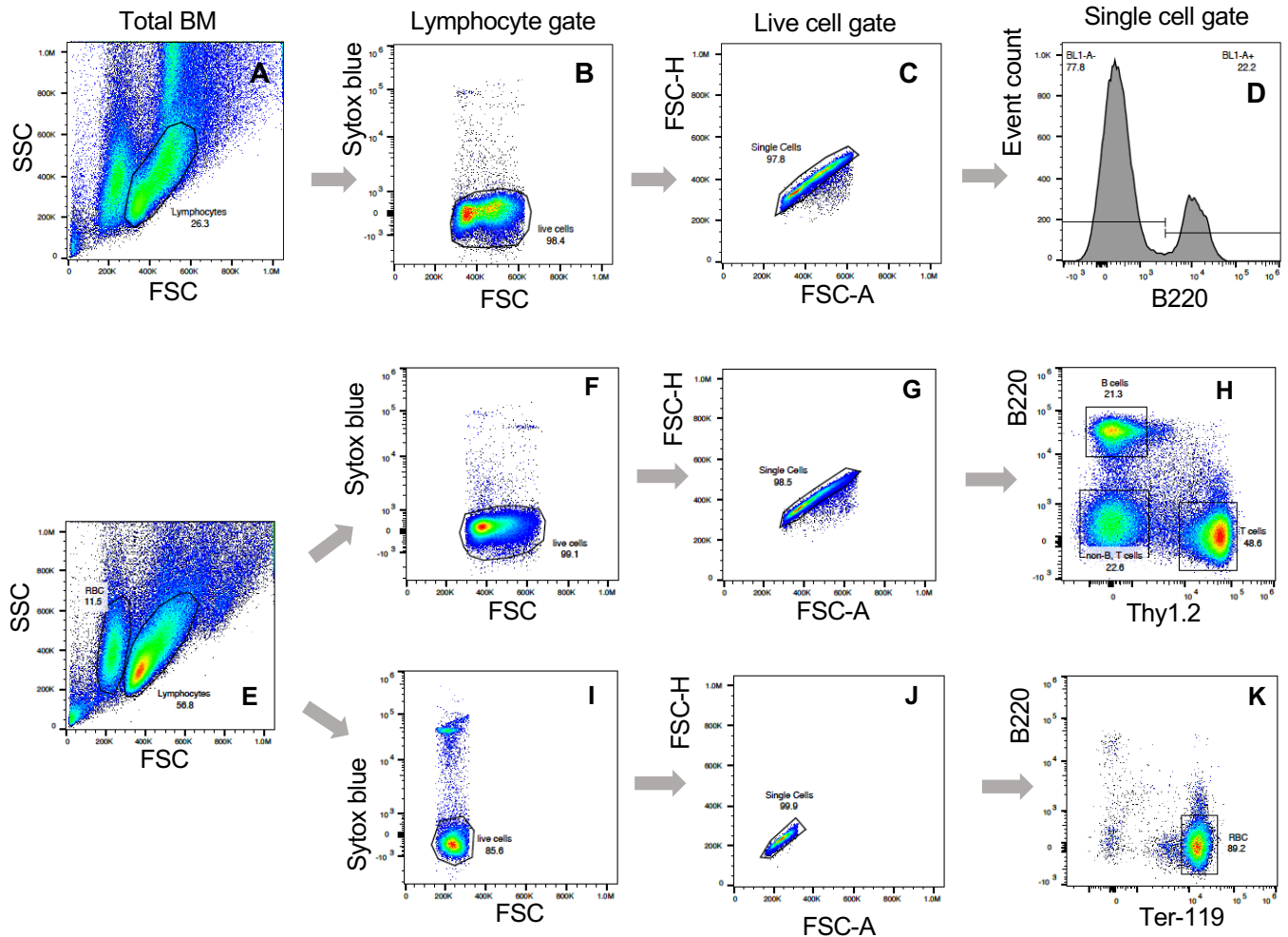
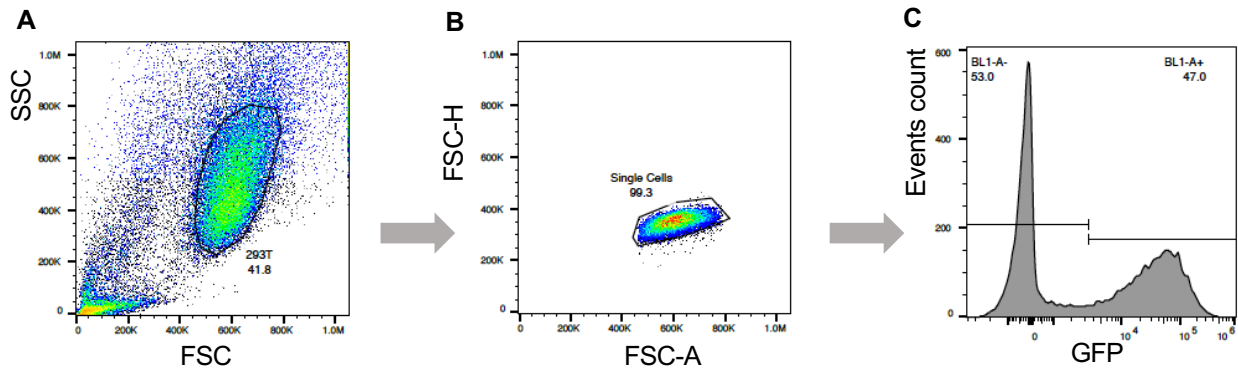


Figure S6



D. GFP+ cells (%) in HC/mVpreB/mλ5 transfection

	Driver	VRC26	VHB1-8
Transfection 1	47.0	39.6	44.0
Transfection 2	47.3	38.2	43.1
Transfection 3	44.0	43.1	41.7
Average	46.1	40.3	42.9

E. GFP+ cells (%) in HC/LC transfection

	Driver	VRC26	VHB1-8
Transfection 1	54.4	49.1	48.9
Transfection 2	47.7	50.7	51.4
Transfection 3	47.7	48.0	48.8
Average	49.9	49.3	49.7

F. GFP+ cells (%) in HC/hVpreB/hλ5 transfection

	Driver	VRC26
Transfection 1	52.2	52.1
Transfection 2	49.0	49.9
Transfection 3	54.2	52.7
Average	51.8	51.6

G. GFP+ cells (%) in HC/hVpreB/mλ5 transfection

	Driver	VRC26
Transfection 1	40.9	38.0
Transfection 2	40.7	40.5
Transfection 3	40.1	38.0
Average	40.6	38.8

H. GFP+ cells (%) in HC/mVpreB/hλ5 transfection

	Driver	VRC26
Transfection 1	53.1	55.0
Transfection 2	54.8	52.0
Transfection 3	53.7	52.0
Average	53.9	53.0

Figures S7

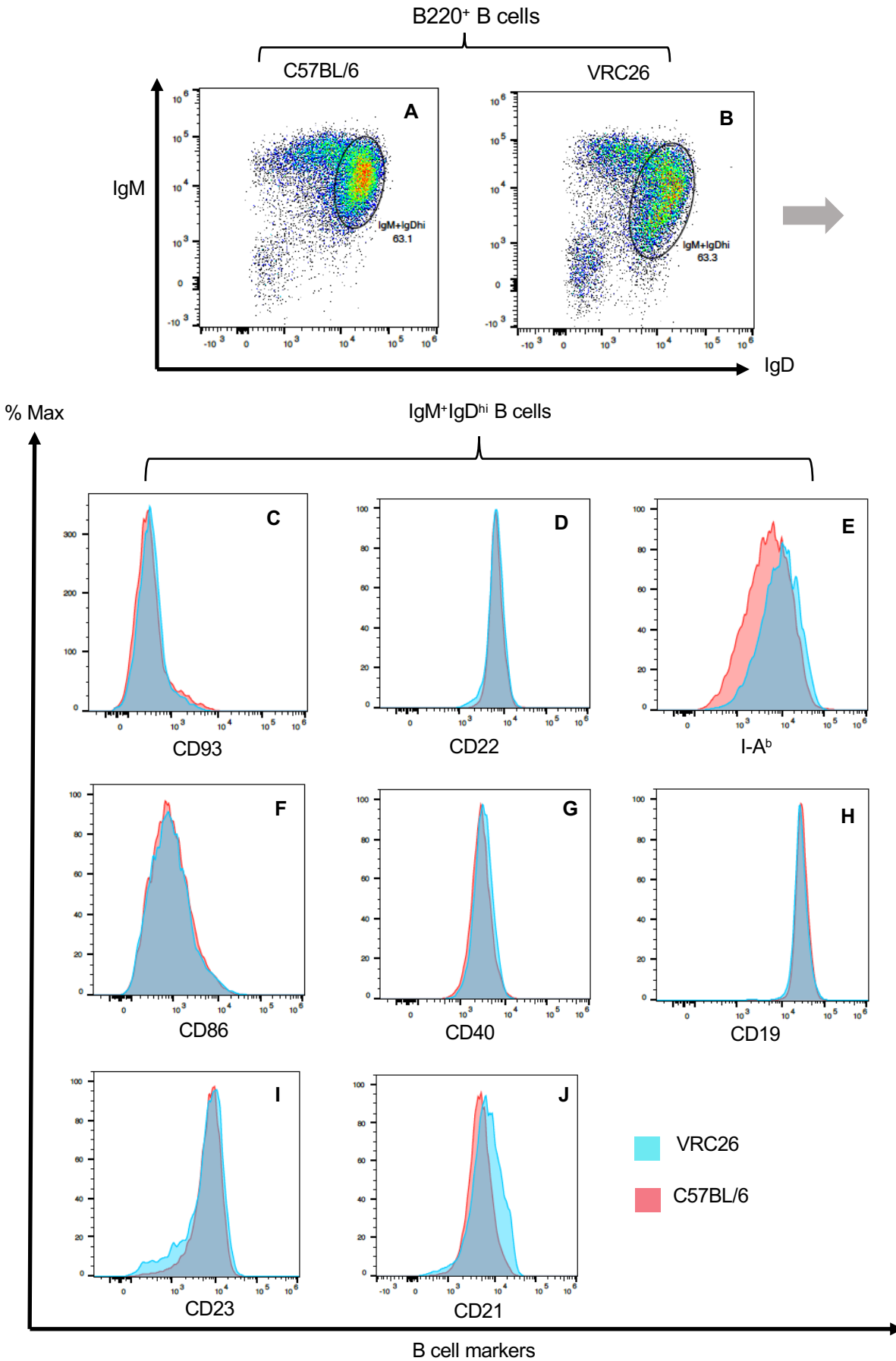


Figure S8

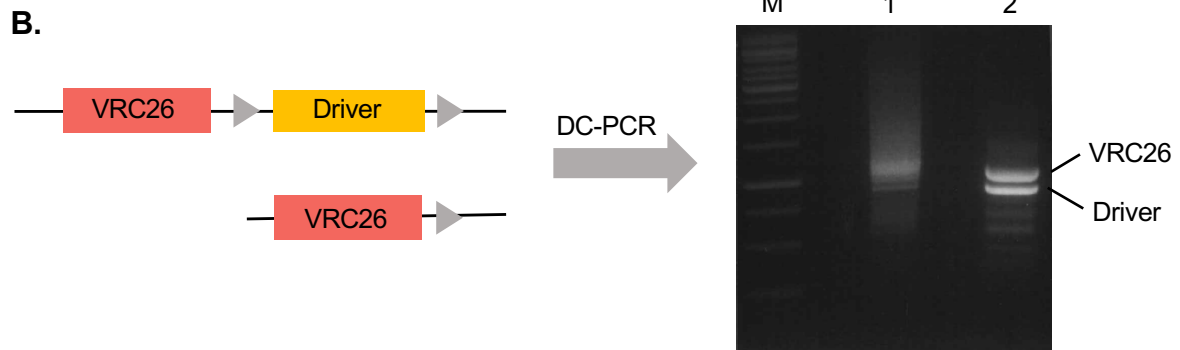
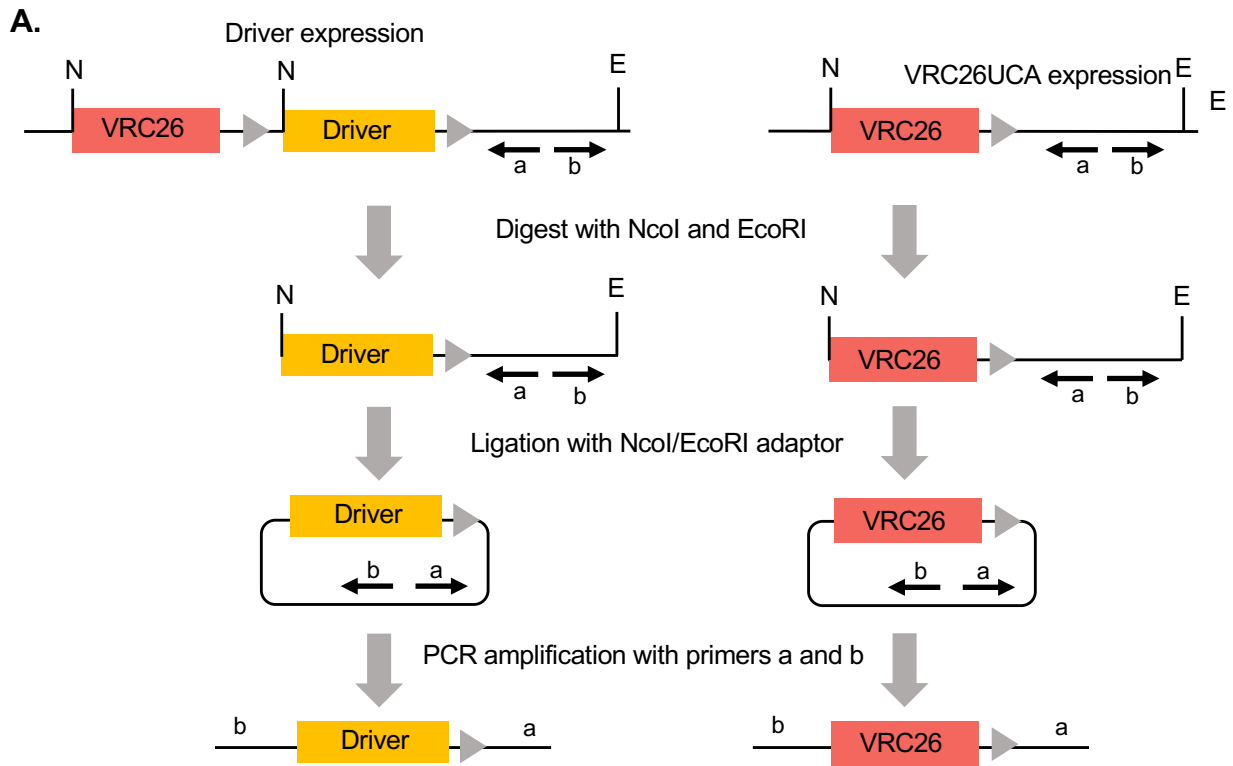


Figure S9

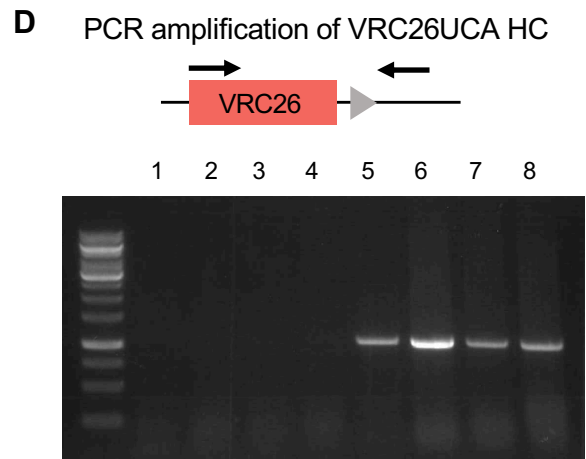
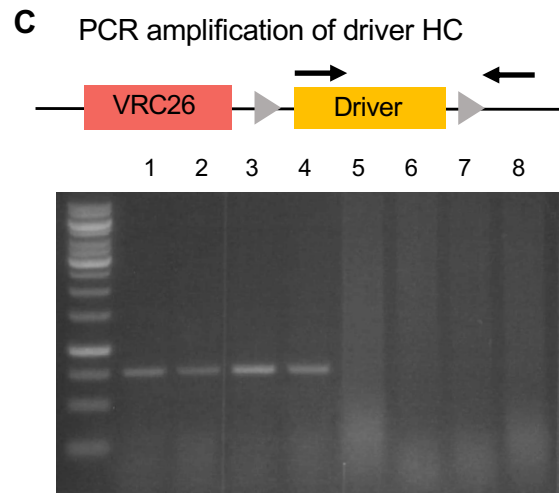
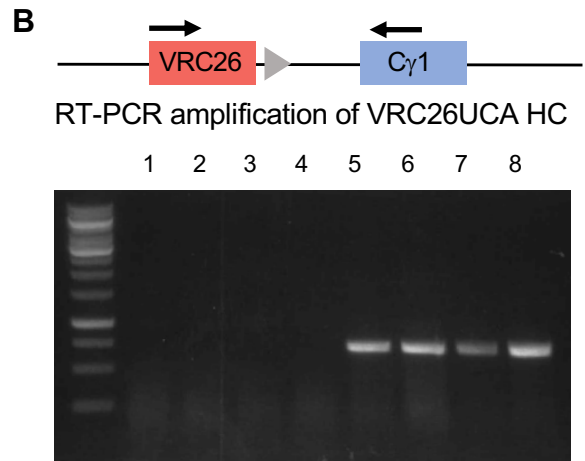
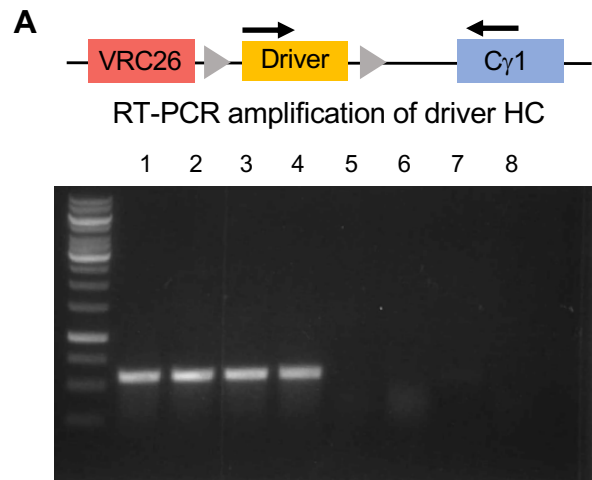


Table S1

Summary of VH replacement events in hybridomas from VRC26UCA KI mouse

Hybridoma clone	Mouse VH	Mouse D	P/NP *	Antibody
1	-	IGHD2-10*02	NP, no VH	IgMb
2	-	IGHD2-3*01	NP, no VH	IgMb
3	-	IGHD2-14*01	NP, no VH	IgMb
4	-	IGHD2-10*02	NP, no VH	IgMb
5	-	IGHD2-10*02	NP, no VH	IgMb
6	-	DSP2.8	NP, no VH	IgG1b
7	VH5-12*02	D2-12*01	NP, out of frame	IgMb
8	IGHV5-6-5*01	IGHD2-2*01	NP, out of frame	IgMb
9	IGHV1S81*02	IGHD2-1*01	NP, out of frame	IgMb
10	IGHV2-7*01	-	NP, out of frame	IgMb
11	IGHV8-2*01	IGHD2-14*01	NP, out of frame	IgG1b
12	IGHV9-2*01	IGHD2-14*01	NP, inframe with stop codon	IgMb
13	IGHV-69*02	-	P	IgG1b
14	IGHV1-26*01#	IGHD2-3*01	P	IgMa
15	IGHV8-12*01	IGH2-4*01	P	IgG1a

* P, productive; NP, non-productive.